Paper Alert

Chosen by Robert Liddington[1] and Christin Frederick[2]

A selection of interesting papers that were published in the month before our press date in major journals most likely to report significant results in structural biology.

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Structure 1998, Vol 6 No 8:1075–1077

☐ **Protein farnesyltransferase: structure and implications for substrate binding.** Peter Dunten, Ursula Kammlott, Robert Crowther, David Weber, Robert Palermo and Jens Birktoft (1998). *Biochemistry* **37**, 7907–7912.

The crystal structure of rat protein farnesyltransferase has been determined. The authors propose a model for substrate binding which differs from the model presented by Park *et al.* based on their independent structure determination. Both farnesyl diphosphate and peptide substrates can be accommodated in the hydrophobic active-site barrel, with the sole charged residue inside the barrel. This model is consistent with mutational studies which have identified several residues critical for substrate specificity and catalysis.
2 June 1998, *Biochemistry*

☐ **Solution structure of the transmembrane H^+-transporting subunit c of the F_1F_0 ATP synthase.** Mark E Girvin, Vinit K Rastogi, Frits Abildgaard, John L Markley and Robert H Fillingame (1998). *Biochemistry* **37**, 8817–8824.

Subunit c is the H^+-translocating component of the F_1F_0 ATP synthase complex. H^+ transport is coupled to conformational changes that ultimately lead to ATP synthesis by the enzyme. Triple resonance NMR experiments were used to determine the complete structure of monomeric subunit c. The protein folds as a hairpin of two antiparallel helical segments, connected by a short structured loop. The shape and charge distribution of the molecular surface of the monomeric protein suggest a packing arrangement for the oligomeric protein in the F_0 complex. (Biochemical evidence for the interaction of subunits a and c was presented by Jiang & Fillingamein *Proc. Natl Acad. Sci. USA* **95**, 6607–6612.)
23 June 1998, *Biochemistry*

☐ **The structure of the monomeric porcine odorant binding protein sheds light on the domain swapping mechanism.** Silvia Spinelli, Roberto Ramoni, Stefano Grolli, Jacques Bonicel, Christian Cambillau and Mariella Tegoni (1998). *Biochemistry* **37**, 7913–7918.

The X-ray structure of the porcine odorant binding protein (OBPp) shows that this lipocalin is a monomer and is devoid of naturally occurring bound ligand, contrary to what was observed in the case of bovine OBP (OBPb). A single glycine insertion in OBPp may prevent domain swapping from taking place. The presence of a disulfide bridge between the OBPp β and α domains may lock it in a nonswapped monomeric conformation. Comparisons with other OBPs indicate that the two cysteines involved in the OBPp disulfide bridge are conserved in the sequence, suggesting that OBPp may be considered a prototypic OBP fold, and not OBPb.
2 June 1998, *Biochemistry*

☐ **NMR solution structure of the 21 kDa chaperone protein DnaK substrate binding domain: a preview of chaperone–protein interaction.** Hong Wang, Alexander V Kurochkin, Yuxi Pang, Weidong Hu, Gregory C Flynn and Erik RP Zuiderweg (1998). *Biochemistry* **37**, 7929–7940.

The solution structure of the 21 kDa substrate-binding domain of the *Escherichia coli* Hsp70 chaperone protein DnaK (DnaK 386–561) has been determined. The domain binds to its own C terminus via a leucine residue that is buried in a deep hydrophobic pocket. A second hydrophobic binding site was identified using paramagnetically labeled peptides and may constitute the allosteric region that links substrate-binding affinity with nucleotide binding in the Hsp70 chaperones.
2 June 1998, *Biochemistry*

☐ **Interaction of polyomavirus internal protein VP2 with the major capsid protein VP1 and implications for participation of VP2 in viral entry.** Xiaojiang S Chen, Thilo Stehle and Stephen C Harrison (1998). *EMBO J.* **17**, 3233–3240.

The crystal structure of a complex of the polyomavirus internal protein VP2/VP3 with the pentameric major capsid protein VP1 has been determined. The C terminus of VP2/VP3 inserts in an unusual, hairpin-like manner into the axial cavity of the VP1 pentamer. The remainder of the internal protein appears to have significant flexibility. This structure restricts possible models for exposure of the internal proteins during viral entry.
15 June 1998, *The EMBO Journal*

☐ **A general module for RNA crystallization.** Adrian R Ferré-D'Amaré, Kaihong Zhou and Jennifer A Doudna (1998). *J. Mol. Biol.* **279**, 621–631.

Crystallization of RNA molecules other than simple oligonucleotide duplexes remains a challenging step in structure determination. The authors have developed a crystallization module consisting of a normally intramolecular RNA–RNA interaction that is recruited to make an intermolecular crystal contact. The target RNA molecule is engineered to contain this module at sites that do not affect biochemical activity. The presence of the crystallization module appears to drive crystal growth, in the course of which other, non-designed contacts are made. The method

has led to group II intron domain crystals that diffract X-radiation to 3.5 Å resolution.
12 June 1998, *The Journal of Molecular Biology*

□ **Structural homologies with ATP- and folate-binding enzymes in the crystal structure of folylpolyglutamate synthetase.** Xiaolin Sun, Andrew L Bognar, Edward N Baker and Clyde A Smith (1998). *Proc. Natl Acad. Sci. USA* **95**, 6647–6652.

Folylpolyglutamate synthetase is responsible for the addition of a polyglutamate tail to folate. The authors report the crystal structure of the MgATP complex of the enzyme from *Lactobacillus casei*. It consists of two domains, one with a typical mononucleotide-binding fold and the other similar to the folate-binding enzyme dihydrofolate reductase. The active site of the enzyme is located in a large interdomain cleft adjacent to an ATP-binding P-loop motif.
9 June 1998, *Proceedings of the National Academy of Science*

□ **Crystal structure of chemically synthesized [N33A] stromal cell-derived factor 1α, a potent ligand for the HIV-1 "fusin" coreceptor.** Chris Dealwis, Elias J Fernandez, Darren A Thompson, Reyna J Simon, Michael A Siani and Elias Lolis (1998). *Proc. Natl Acad. Sci. USA* **95**, 6941–6946.

Stromal cell-derived factor 1α (SDF-1α) is a member of the chemokine superfamily and functions as a growth factor and chemoattractant through activation of CXCR4/LESTR/Fusin, a G-protein-coupled receptor. This receptor also functions as a coreceptor for T-cutain strains of HIV-1. SDF-1α antagonizes infectivity of these strains by competing with gp120 for binding to the receptor. The crystal structure of a variant SDF-1α ([N33A]SDF-1α) prepared by total chemical synthesis has been determined. Although SDF-1α adopts a typical chemokine β-β-β-α topology, the packing of the α helix against the β sheet is strikingly different.
9 June 1998, *Proceedings of the National Academy of Science*

■ **Structure of an HIV gp120 envelope glycoprotein in complex with the CD4 receptor and a neutralizing human antibody.** Peter D Kwong, Richard Wyatt, James Robinson, Raymond W Sweet, Joseph Sodroski and Wayne A Hendrickson (1998). *Nature* **393**, 648–659.

The entry of human immunodeficiency virus (HIV) into cells requires the sequential interaction of the viral exterior envelope glycoprotein, gp120, with the CD4 glycoprotein and a chemokine receptor on the cell surface. The crystal structure of an HIV-1 gp120 core complexed with a two-domain fragment of human CD4 and an antibody that blocks chemokine–receptor binding reveals a cavity-laden CD4–gp120 interface, a conserved binding site for the chemokine receptor, evidence for a conformational change upon CD4 binding, and specific mechanisms for immune evasion.
18 June 1998, *Nature*

□ **Structure of a heparin-linked biologically active dimer of fibroblast growth factor.** Anna D DiGabriele, Irit Lax, Denise I Chen, Carl M Svahn, Michael Jaye, Joseph Schlessinger and Wayne A Hendrickson (1998). *Nature* **393**, 812–817.

The fibroblast growth factors (FGFs) mediate cellular functions by binding to transmembrane FGF receptors. FGF receptors are activated by oligomerization which requires heparin-like molecules as well as FGF. The authors describe the crystal structure of a biologically active dimer of human acidic FGF in a complex with a fully sulphated, heparin decassacharide. The dimerization of heparin-linked acidic FGF provides a mechanism for the modulation of signalling through combinatorial homodimerization and heterodimerization of the 12 known members of the FGF family.
25 June 1998, *Nature*

□ **Structural basis for the interaction of Ras with RalGDSI.** Lan Huang, Franz Hofer, G Steven Martin and Sung-Hou Kim (1998). *Nat. Struct. Biol.* **5**, 422–426.

The Ras protein signals to a number of distinct pathways by interacting with diverse downstream effectors. Among the effectors of Ras are the Raf kinase and RalGDS, a guanine nucleotide dissociation stimulator specific for Ral. The authors report the 2.1 Å crystal structure of the complex between Ras and the Ras-interacting domain (RID) of RalGDS. The β sheet of the RID joins the switch I region of Ras to form an extended β sheet with a topology similar to that found in the Rap–Raf complex. The sidechain interactions and the relative orientation of the two binding domains are distinctly different, however.
June 1998, *Nature Structural Biology*

□ **Solution structure of the thermostable sweet-tasting protein brazzein.** Jane E Caldwell, Frits Abildgaard, Zeljko Dzakula, Ding Ming, Göran Hellekant and John L Markley (1998). *Nat. Struct. Biol.* **5**, 427–431.

The fruit of *Pentadiplandra brazzeana* Baillon contains a small, sweet-tasting protein named brazzein. The solution structure was determined by NMR spectroscopy. The brazzein fold, which contains one α helix and three strands of antiparallel β sheet, does not resemble that of either of the other two sweet-tasting proteins with known structures, monellin and thaumatin. Instead, the structure resembles those of plant γ-thionins and defensins and arthropod toxins.
June 1998, *Nature Structural Biology*

□ **Structure of the dimer initiation complex of HIV-1 genomic RNA.** Anwer Mujeeb, Jared L Clever, Todd M Billeci, Thomas L James and Tristram G Parslow (1998). *Nat. Struct. Biol.* **5**, 432–436.

Retroviral genomes must dimerize to be fully infectious. Dimerization is directed by a unique RNA hairpin structure with a palindrome in its loop: hairpins of two strands first

■ See the Minireview article by Quentin Sattentau in this issue of *Structure* (pages 1075–1077).

associate transiently through their loops, and then refold to a more stable, linear duplex. The structure of the kissing-loop dimer from HIV-1, solved using 2D NMR, is bent and metastable, its interface being formed not only by standard base pairing between palindromes, but also by a distinctive pattern of interstrand stacking among bases at the stem-loop junctions.
June 1998, *Nature Structural Biology*

☐ **Crystal structure of calsequestrin from rabbit skeletal muscle sarcoplasmic reticulum.** Shuren Wang, William R Trumble, Hong Liao, Carla R Wesson, A Keith Dunker and ChulHee Kang (1998). *Nat. Struct. Biol.* **5**, 476–483.
The authors have determined the structure of rabbit skeletal muscle calsequestrin, the major Ca^{2+} storage protein of muscle. Three very negative thioredoxin-like domains surround a hydrophilic center. Each monomer makes two extensive dimerization contacts, both of which involve the approach of many negative groups. This structure suggests a mechanism by which calsequestrin may achieve high capacity Ca^{2+} binding involving Ca^{2+}-induced collapse of the three domains and polymerization of calsequestrin monomers.
June 1998, *Nature Structural Biology*

☐ **A new DNA-binding motif in the Skn-1 binding domain–DNA complex.** Peter B Rupert, Gary W Daughdrill, Bruce Bowerman and Brian W Matthews (1996). *Nat. Struct. Biol.* **5**, 484–491.
The DNA-binding domain of Skn-1, a developmental transcription factor that specifies mesoderm in *Caenorhabditis elegans*, is shown by X-ray crystallography to have a novel fold in which a compact, monomeric, four-helix unit organizes two DNA-contact elements. At the C terminus, a helix extends from the domain to occupy the major groove of DNA in a manner similar to bZip proteins. Skn-1 lacks the leucine zipper found in all bZips but additional contacts with the DNA are made by a short basic segment at the N terminus of the domain, reminiscent of the 'homeodomain arm'.
June 1998, *Nature Structural Biology*

☐ **Redox-coupled crystal structural changes in bovine heart cytochrome *c* oxidase.** Shinya Yoshikawa, Kyoko Shinzawa-Itoh, Ryosuke Nakashima, Rieko Yaono, Eiki Yamashita, Noriko Inoue, Min Yao, Ming Jie Fei, Clare Peters Libeu, Tsunehiro Mizushima, Hiroshi Yamaguchi, Takashi Tomizaki and Tomitake Tsukihara (1998). *Science* **280**, 1723–1729.
Crystal structures of bovine heart cytochrome *c* oxidase in the fully oxidized, fully reduced, azide-bound, and carbon monoxide-bound states have been determined. This complete series of structures allows for a detailed description of the mechanism of O_2 reduction. An aspartate residue distant from the O_2 reduction site changes its accessibility from the matrix aqueous phase to the cytosolic phase on reduction of the metal sites. The movement indicates the aspartate as the proton pumping site. A tyrosine acidified by a covalently linked imidazole nitrogen is a possible proton donor.
12 June 1998, *Science*

☐ **The structure of immunoglobulin superfamily domains 1 and 2 of MAdCAM-1 reveals novel features important for integrin recognition.** Kemin Tan, Jose M Casasnovas, Jin-huan Liu, Michael J Briskin, Timothy A Springer and Jia-huai Wang (1998). *Structure* **6**, 793–801.
Mucosal addressin cell adhesion molecule 1 (MAdCAM-1) binds both the integrin $\alpha4\beta7$, through its two IgSF domains, and a selectin expressed on leukocytes, via carbohydrate sidechains. The crystal structure of a fragment containing the two IgSF domains shows that MAdCAM-1, like VCAM-1, has the key integrin-binding residue located on the protruding CD loop of domain 1. Architectural differences in the CD loops of MAdCAM-1 and VCAM-1 cause an 8 Å shift in position of the critical aspartate residue, and may partly determine their binding preference for different integrins. The unusual charge distribution of the two-domain fragment of MAdCAM-1 is predicted to orient the molecule optimally for integrin binding.
15 June 1998, *Structure*